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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/484,879	01/18/2000	Vernon L. Alvarez		1229

20583 7590 04/08/2003

PENNIE AND EDMONDS  
1155 AVENUE OF THE AMERICAS  
NEW YORK, NY 100362711

[REDACTED] EXAMINER

CELSA, BENNETT M

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1639

DATE MAILED: 04/08/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

*file copy*

## Office Action Summary

Application No. <b>09/484,879</b>	Applicant(s) <b>Alvarez, V.L.</b>
Examiner <b>Bennett Celsa</b>	Art Unit <b>1639</b>

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1)  Responsive to communication(s) filed on Jan 14, 2003.
- 2a)  This action is FINAL.      2b)  This action is non-final.
- 3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.
- 4)  Claim(s) 2-4, 6, 8, 10, 27, 30, 36, 45, 47, and 48 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5)  Claim(s) \_\_\_\_\_ is/are allowed.
- 6)  Claim(s) 2-4, 6, 8, 10, 27, 30, 36, 45, 47, and 48 is/are rejected.
- 7)  Claim(s) \_\_\_\_\_ is/are objected to.
- 8)  Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

Application Papers

- 9)  The specification is objected to by the Examiner.
- 10)  The drawing(s) filed on \_\_\_\_\_ is/are a)  accepted or b)  objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner. If approved, corrected drawings are required in reply to this Office action.
- 12)  The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13)  Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a)  All b)  Some\* c)  None of:
1.  Certified copies of the priority documents have been received.
  2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
- a)  The translation of the foreign language provisional application has been received.
- 15)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1)  Notice of References Cited (PTO-892)
- 2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
- 4)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5)  Notice of Informal Patent Application (PTO-152)
- 6)  Other: \_\_\_\_\_

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## **DETAILED ACTION**

### ***Response to Amendment***

Applicant's amendment dated 1/14/03 in paper no. 14 is acknowledged.

### ***Status of the Claims***

Claims 2-4, 6, 8, 10, 27, 30, 36, 45, 47 and 48 are pending.

Claims 2-4, 6, 8, 10, 27, 30, 36, 45, 47 and 48 are under consideration.

**NOTE:** the location of the present application is ART UNIT 1639.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Withdrawn Objection (s) and/or Rejection (s)***

Applicant's amendment has overcome the nonstatutory rejection of claims 2-4, 6, 8, 10, 27, 30, 36 and 45 are rejected under 35 U.S.C. 101.

Applicant's amendment has overcome the indefinite rejection of claim 45.

### ***Outstanding Objection(s) and/or Rejection (s)***

2. Claims 2-4, 6, 8, 10, 27, 30, 36, 45, 47 and 48 are rejected under 35 U.S.C. 102(a,b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Griffiths et al. WO 93/11236 (6/93) .

Present claims 2-4, 6, 8, 10, 27, 30, 36 and 45 are drawn to "product by process claims" which define the product solely by its method of making (e.g. screening). See MPEP 2113 directed to "Product by Process Claims". Even though product - by process claims are limited

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by and defined by the process, determination of patentability is *based on the product itself*. The patentability of a product does not depend on its method of production. If the product in the product - by - process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe* , 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the Examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi*, 218 USPQ 289, 292 (Fed. Cir. 1983). When the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product - by - process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown* , 173 USPQ 685, 688 (CCPA 1972)

The present claims (claims 2-4, 6, 8, 10, 27, 30, 36, 45, 47 and 48) are directed to  
A compound *comprising*:

- A. A peptide of *about 10-100 amino acids* ( e.g. claim 2 and dependent claims and compositions thereof e.g. claim 27) or
- B. *about 20-50 amino acids* (e.g. new claims 47-48)

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which "mimics" the binding specificity of an antibody

C. The above compounds further may possess the ability to "mimic" the binding specificity of an antibody that binds a human tumor antigen (e.g. claim 45), such as a monoclonal antibody (e.g. 7E11-C5) which binds human prostate carcinoma cell line LNCap (e.g. claim 8).

D. All of the above compounds comprise peptides of about 10-100 or about 20-50 amino acids which are screened from two successive random peptide libraries.

Griffiths disclose peptides which are "anti-self antibody fragments" (e.g. scFv, Fd, Fab or *any other fragment* which has the capability of binding antigen) which bind "self antigens".

Accordingly, the Griffith antibody peptide fragments are "**compounds comprising** a peptide of *about 10-100 amino acids* (or *about 20-50 amino acids*) which mimics the binding specificity of an antibody" since the fragments mimic the ability of the parent antibody (monoclonal/polyclonal) to bind the same antigen (e.g. see abstract; examples and claims); and clearly would "comprise" *about 10-100 amino acids* (or *about 20-50 amino acids*) as presently claimed..

To the extent that patentable weight is given the limitation "capable of specifically binding to a human tumor antigen" due to the product-by process format and the use of "capable of" ; the reference antibody fragments, nevertheless anticipate, since these peptides can be made "capable of specifically binding to a human tumor antigen" if the phage library is screened against a tumor antigen; or if the peptide is derivatized to enable tumor binding (e.g conjugated to antibody that targets a tumor antigen). Additionally, since not all tumor antigens are known, the ability of a particular reference peptide to bind or not bind a tumor cell can only be determined through

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assaying each of the reference peptides; since any one of the reference peptides may possess the inherent ability to bind a tumor cell via an antigen to some degree. Accordingly, all of the reference screened peptides are potentially "capable of binding a human tumor antigen" to some degree; the degree of which must be determined by screening.

Further, the reference teaches the making of anti CEA (human) scFv antibodies (e.g. see pages 46-49, lines page 75 and Table 1). Since human carcinoembryonic antigen (CEA) is "a human tumor antigen" the reference teaches a peptide (e.g. scFV antibody) which specifically binds (e.g. and therefore is capable of binding) a human tumor antigen (human CEA); and which also mimics the binding specificity of an antibody (e.g. an anti-CEA monoclonal or polyclonal antibody) and thus anticipates claims 2-4, 6, 8, 10, 27, 30, 36 as well as claim 45.

### ***Discussion***

Applicant's arguments directed to the above anticipation rejection were considered but deemed nonpersuasive for the following reasons. Initially, it is noted that the above rejection was modified in response to applicant's amendment.

Applicant argues that amending the claims to "recite a peptide of about 10 to 100 amino acids (or about 20 to 50 amino acids)" distinguishes over the use by Griffiths of antibody fragments formed from " $V_H$  or  $V_L$ ,  $V_LC_L$ ,  $V_HC_H1$ , scFv fragments, Fab fragments" which are asserted to be larger than 100 amino acids as supported by textbook references referring to VH or VL domains being "about 110 amino acids" (VH/VL asserted to be the smallest in size).

This argument was considered but deemed nonpersuasive for several reasons.

Applicant's arguments are not commensurate in scope to the presently claimed invention.

The claims are drawn to "compounds comprising a peptide of about 10 to 100 amino (or about 20 to 50 amino acids) which mimics the binding specificity of an antibody".

Accordingly, use in the presently claimed invention of the term "**comprise**" includes compounds with additional peptide structure beyond about 10-100 amino acids and thus would include the entire "V<sub>H</sub> or V<sub>L</sub>, V<sub>L</sub>C<sub>L</sub>, V<sub>H</sub>C<sub>H</sub>1, scFv fragments, Fab fragments" structure. This is consistent with the specification (page 23) which includes additional amino acid structure as composing an "abtide".

Secondly, even assuming arguendo, applicant is correct regarding the size of the various single chain antibody domains, the present invention would encompass peptides of "**about** 100 amino acid" which is within the scope of the size of an individual V<sub>H</sub> or V<sub>L</sub> domain (e.g. "**about** 110 amino acids") .

Thirdly, the Griffith reference specifically teaches peptides with antigen binding affinity which are "fragments" of antibody domains (e.g. V<sub>H</sub> or V<sub>L</sub> domain). See e.g. Examples 3 and 4 which teaches antibody fragments derived from V genes which possess high antigen specificity. Accordingly, the Griffith reference clearly teach "abtides" which are smaller than "about 110 amino acids".

Accordingly, the Griffith method produces "compounds" that comprise peptides about 10 to 100 amino (or about 20 to 50 amino acids) which "mimic" the binding specificity of an antibody (e.g. to a cancer antigen). The compounds produced by the Griffith method appear to

be the same (or substantially identical ) to the compounds produced by the presently claimed method.

Even though product - by process claims are limited by and defined by the process, determination of patentability is *based on the product itself*. The patentability of a product does not depend on its method of production. If the product in the product - by - process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe* , 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). The Examiner has provides several rationales which tend to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process; thus the *burden shifts to applicant* to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi*, 218 USPQ 289, 292 (Fed. Cir. 1983). . *As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith.*" *In re Brown* , 173 USPQ 685, 688 (CCPA 1972)

Accordingly, for all of the above reason, the above anticipation rejection, as modified, is hereby retained.

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***New Objection (s) and/or Rejection (s)***

3. Claims 2-4, 6, 8, 10, 27, 30, 36, 45, 47 and 48 are rejected under 35 U.S.C. 102(a,b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Renschler et al. Proc. Nat'l Acad. Sci. USA Vol. 91 (April 1994) pages 3623-3627.

Present claims 2-4, 6, 8, 10, 27, 30, 36 and 45 are drawn to "product by process claims" which define the product solely by its method of making (e.g. screening). See MPEP 2113 directed to "Product by Process Claims". Even though product - by process claims are limited by and defined by the process, determination of patentability is *based on the product itself*. The patentability of a product does not depend on its method of production. If the product in the product - by - process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the Examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi*, 218 USPQ 289, 292 (Fed. Cir. 1983). When the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product - by - process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then

obtain prior art products and make physical comparisons therewith." *In re Brown*, 173 USPQ 685, 688 (CCPA 1972)

The present claims (claims 2-4, 6, 8, 10, 27, 30, 36, 45, 47 and 48) are directed to A compound *comprising*:

- A. A peptide of *about 10-100 amino acids* (e.g. claim 2 and dependent claims and compositions thereof e.g. claim 27) or
- B. *about 20-50 amino acids* (e.g. new claims 47-48)  
which "mimics" the binding specificity of an antibody
- C. The above compounds further may possess the ability to "mimic" the binding specificity of an antibody that binds a human tumor antigen (e.g. claim 45), such as a monoclonal antibody (e.g. 7E11-C5) which binds human prostate carcinoma cell line LNCap (e.g. claim 8).
- D. All of the above compounds comprise peptides of about 10-100 or about 20-50 amino acids which are screened from two successive random peptide libraries.

The Renschler et al. reference discloses peptide ligands (isolated from 8mer and 12mer phage libraries) which "mimic" the binding of antibodies (e.g. "Abtides") that bind a human tumor antigen (e.g. immunoglobulin receptor of B-cell lymphomas). The reference further teaches "compounds that comprise" the peptide ligands 8mer/12mer which include dimers (e.g. at least 16 to 24 amino acids) and tetramers (e.g. at least 32-48 amino acids) of these ligands which constitute abtides within the scope of the presently claimed invention. E.g. see Tables 1-2; figures 1-5; 30 amino acid "tandom repeat form of peptide C" (including peptide C 12 amino acid dimers

linked by 6 glycines) see pages 3625-3626 described peptide dimers and tetramers; Fig. 3a showing peptide tetramer IC<sub>50</sub> of 60-200nM which represents "specific" binding. The reference peptides are formulated in compositions which comprise a "carrier" (e.g. pharmaceutically acceptable) within the scope of the presently claimed invention or alternatively the reference would render obvious the combination of such peptides with carriers since the reference teaches the use of these peptide ligands, *particularly the "multimeric" forms*, in human assays or therapy (e.g. see page 3623, left column and page 3627 e.g. conjugated to deliver toxins or radionuclides). These peptides are advantageous : E.g. "[T]he tissue penetration of peptides, the ease of synthesis, and the ability to modify peptides are superior to antibodies. Finally, peptides tend to be less immunogenic than monoclonal antibodies." (See page 3623). Accordingly, the Renschler et al. reference teaches Abtides which "comprise" about 8-48 **or more** (e.g. especially with the use of glycine linkers in multivalent forms) amino acids which "mimic" antibodies that bind human tumor antigens (e.g. B-cell lymphomas) within the scope of the presently claimed invention. Since not all tumor antigens are known, the ability of a particular reference peptide to bind or not bind a different tumor cell antigen (e.g. "mimic" the binding of monoclonal antibody 7E11 with LNCap) can only be determined through assaying each of the reference peptides; since any one of the reference peptides may possess the inherent ability to bind a different tumor cell antigen *to some degree*. Accordingly, all of the reference screened peptides mimic the binding of antibodies to tumor cell antigens (e.g. B-cell lymphomas) and are potentially "capable of"

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binding a different human tumor antigen" (e.g. human prostate carcinoma cell line LNCap) to some degree; the degree of which must be determined by screening.

### Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang (art unit 1639), can be reached at (703)306-3217.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1639)  
April 2, 2003

BENNETT CELSA  
PRIMARY EXAMINER

